Applicants further elect, with traverse, as required, the species:

1) the ECM inhibiting agent: ACE inhibitors (Claims 4, 6, 27, 39 and 50);
2) the ECM degrading agent: protease (Claims 9-14, 20, 38, 40, 43-48 and 53-54);
3) the agent that increases the amount of active protease: tPA (Claims 13, 44 and 47);
4) the fibrotic condition to be treated: diabetic kidney disease (Claim 16).

Traversal of The Restriction Requirements

The Office divided pending Claims 1-55 into Groups I-IV, and stated that the inventions listed in these groups "do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The prior art, as evidenced by the search report for the instant application, has shown that there were a plethora of known inhibitors for inhibiting TGFß to decrease ECM, see Border et al. [Nature Vol. 360:361-364, 1992] for example. This reference destroys the novelty of claim 32, for example and thus destroys any special technical feature of the claimed invention." (Office Action, page 3).

Applicants first note that claim 32 was amended (Communication to WIPO dated August 4, 2000) so that Claim 32 as amended now reads:

> 32. A method for preventing or reducing excess extracellular matrix accumulation in a tissue or organ at a wound site comprising inhibiting the overproduction of TGFß present in an organ or tissue or at a wound site to prevent the excess accumulation of extracellular matrix by administering a combination of agents that inhibit TGFß activity and/or production.

The Office asserts that because there were known inhibitors for inhibiting TGFß to decrease ECM, the novelty of Claim 32 is destroyed, and thus there are no "special technical features" of the invention claimed in Claim 32. (Office Action, page 3).

As amended, Claim 32 recites the administration of a "combination of agents that inhibit TGFß activity and/or production." The novelty of Claim 32 lies in the use of a combination of agents that inhibit TGFß. None of the references teach the use of a combination of TGFß inhibiting agents, and thus the novelty of Claim 32 is not destroyed.

Applicants submit, that Claims 1-31 and 55 (Group I), Claims 32-34 (Group II) and Claims 52-54 (Group IV) relate to a single general inventive concept because they share technical features. All of these claims are directed to methods which prevent or reduce the excess accumulation of extracellular matrix (ECM), by 1) reducing ECM associated with TGFß overproduction and degrading excess accumulated ECM (Claims 1, 21, 33), by using at least one agent that inhibits TGFß (Claims 2-8), **and** at least one agent (a protease) to degrade excess ECM (Claims 9-14, and Claim 55); **or** by using 2) a combination of agents that inhibit TGFß (Claims 26-31, and Claim 32), **or** by using 3) at least one agent to degrade excess ECM (Claims 52-54). The shared technical features of these claims are the use of agents, and combinations of agents, to prevent and reduce excess ECM by inhibiting TGFß, and/or by degrading excess ECM.

Because of the commonality between these claims (Groups I, II and IV), no additional resources of the Office need be directed to search and examination of these claims together in a single application.

With respect to the claims of Group III, Claims 35-51, these claims are directed to compositions of the agents set forth in the methods of the claims of Groups I, II and IV. Because the agents are common technical features of the claims of Group III and Groups I, II and IV, the claims of Group III should be examined together with the claims of Groups I, II and IV in a single application.

Traversal of the Species Requirement

The Office also required election of species, i.e. various agents and a fibrotic condition to be treated, as follows:

1) an ECM inhibiting agent;
2) an ECM degrading agent;
3) an agent that increases the amount of active protease; and
4) the fibrotic condition to be treated.

The Office asserts that the species lack unity of invention because "they are not so linked as to form a single general inventive concept under PCT Rule 13.1" (Office Action, page 3). The Office further comments that each species "is [a] compound that differes [sic]from the others in that they do not share the same structure and function,. For example the inhibitors range vastly in the mechanisms of action in that one may bind to the protein and inhibit its action while another may act indirectly to inhibit its action. The diseases contemplated differe [sic]in that the disease states manifest in different manners where the disease may be caused by an indirect action on or may be caused by an over expression of a normal TGFß or a mutant TGFß, for example. Further more the special technical feature of the claimed invention has been destroyed by the prior art." (Office Action, pages 4-5).

Applicants reiterate that the special technical features (novelty) of the claimed invention has not been destroyed by the prior art, for the reasons set forth above. Applicants further submit that the species of agents are related as 1) TGFß-inhibiting agents; 2) ECM degrading agents; and 3) agents that increase the amount of active protease. The fact that within each category of action, the compounds may differ structurally does not destroy their relation to the single general inventive concept of their function as either TGFß inhibitors, ECM degraders or protease enhancers, and their use in the methods of the invention, i.e. to prevent or reduce excess ECM accumulation.

With respect to the fibrotic condition to be treated, the fibrotic conditions recited in Claim 16 share the technical feature of association with excess accumulation of ECM as a result of TGFß overproduction.

CONCLUSION

Applicants submit that all the claims of the application (Claims 1-55) relate to a single general inventive concept as required under PCT Rule 13.1, and share common special technical features. As such, Applicants request that Claims 1-55 be examined together in a single application.

If any additional fees are necessary, the Patent Office is authorized to charge the additional fees to Deposit Account No. 50-0306.

Respectfully submitted,

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